BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellant(s): Annaliesa S. Anderson, *et al.*

Application Number: 10/564,458

Filing Date: January 12, 2006

Title of the Invention: POLYPEPTIDES FOR INDUCING A PROTECTIVE IMMUNE RESPONSE AGAINST STAPHYLOCOCCUS AUREUS

Examiner: Devi, Sarvamangala

Art Unit: 1645

APPELLANTS REPLY BRIEF

INTRODUCTION

The Examiner's Answer maintains all the pending rejections. The pending rejections are directed to 35 U.S.C. § 112, first paragraph (written description) and 35 U.S.C. § 112, second paragraph (definiteness). In addition, several of the claims were objected to.

Appellants Appeal Brief included different groups of claims that were argued separately. The Examiner's Answer, particularly in the written description section, does not appear to present separate arguments for different groups of claims. Appellants continue to argue separately the different groups of claims as provided in Appellants Appeal Brief.

APPELLANTS RESPONSE

I. Claims 1, 4, 7-9, 33-35, 38-44 and 49-51 Comply with 35 U.S.C. § 112, first paragraph (Written Description)

The data provided in the application reasonably conveys to one of ordinary skill in the art that applicants were in possession of the claimed invention when the application was filed. The Examiner's Answer fails to consider all of the data submitted to the Office, and attempts to support the written description rejection by making arguments mischaracterizing the heterologous protection data provided in the application.

The Office correctly acknowledges that based on the ability of the longer-length SEQ ID NO: 28 sequence to provide protection against a *S. aureus* challenge strain, the skilled artisan would have expectations concerning the ability of the ORF0657nI region present in the challenge strain to provide protection against *S. aureus*. (See, Appellants Response I.C. *infra.*) However, the Office erroneously argues that SEQ ID NO: 28, and the corresponding ORF0657nI region, "induces" a high level of cell death. (See, Appellants Response I.B. and I.C. *infra.*) Cell death is caused by the *S. aureus* challenge strain, not the antigen.

The data in the application demonstrates that animals vaccinated with SEQ ID NO: 28 has an enhanced survival compared to animals not receiving the vaccine. (See, Appellants Response I.B. *infra.*) Such data helps demonstrates that SEQ ID NO: 1 is representative of the claimed species and that the prophetic examples of different ORF0657nI region described in the application would also be protective. (See, for example, Appellants Appeal Brief Argument I.A.3. discussing Example 6 protection data.)

Appellants' response to the Office's written description rebuttal arguments are provided

below. Appellants Response at section I.A. summarizes the data provided in the application supporting written description. Appellants Response at sections I.B. and I.C., highlight the new arguments presented by Office concerning SEQ ID NO: 28, and the relevance of the data obtained with SEQ ID NO: 28 to expectations for using the ORF0657nI region from the challenge strain as an protective antigen. Appellants Response at section I.D. addresses the different arguments made throughout the Office Rebuttal.

A. Data Provided in the Application Supporting Written Description

The present application reasonable conveys to one skilled in the art possession of the polypeptide immunogen described in the claims by providing heterologous protection data using different challenge strains, and by providing sequence information on different strains. The provided protection data includes data demonstrating the ORF0657nI region of SEQ ID NO: 1 is sufficient to provide protection against *S. aureus*, and provides evidence the ORF0657nI region present in different challenge strains would also provide protection against *S. aureus*. (Appellants Appeal Brief Argument I. at pages 8-16.)

The ability of SEQ ID NO: 28 to provide protection against different *S. aureus* clinical isolates provides evidence that SEQ ID NO: 1 is representative of the claimed species and that the prophetic examples of different ORF0657nI region described in the application would also be protective. The prophetic examples of ORF0657nI region include the ORF0657nI region from CL-10, CL-11, CL-13, CL-18, CL-21, and CL30, for which protection was shown using SEQ ID NO: 28. (See, for example Appellants Appeal Brief Argument I.A.3. discussing Example 6 protection data.)

B. Office Arguments Mischaracterizing SEQ ID NO: 28 as Inducing "Death"

The Examiner's Answer incorrectly asserts that the SEQ ID NO: 28 polypeptide induces "death". For example, the Office argues:

> The SEQ ID NO: 28 polypeptide, upon administration to mice in an immune-sufficient mouse model of *S. aureus* infection, **induced approximately 80% death** (not 80% survival) of the animals immunized therewith, following challenge infection with one of the three different isolates of *S. aureus*, CL-10, CL-13, and CL-18. See Figures 4A, 4D, and 4G. The SEQ ID NO: 28 polypeptide showed a death rate almost equal to the one induced in control mice

> immunized with AHP adjuvant alone. See Figure 4A. Accordingly, a longer than full-length polypeptide **causing about 80% death** of the immunized mice or showing a death rate almost equal to the one induced in control mice immunized with an adjuvant alone, is not viewed by those of skill in the art as a polypeptide immunogen conferring *protection* to heterologous isolates of *S. aureus* and as a polypeptide immunogen representative of the claimed broad genus of protective polypeptide or immunogen variants. [Bold emphasis added.]

(Examiner's Answer page 53, lines 7-21.) The Office had not previously presented any arguments concerning the CL-10, CL-13, and CL-18 data.

The conclusion concerning SEQ ID NO: 28 inducing a high level of death is based on a misunderstanding of the experiment. Cell death is caused by the *S. aureus* challenge strain. The SEQ ID NO: 28 antigen does not induce "cell death", as asserted by the Office. As pointed out by the present application, the employed animal model system measures the ability of a polypeptide to provide protection against *S. aureus.* (See, the present application at pages 21-22, section titled "Animal Model System".)

The data shown in Figures 4A-4H of the present application provides clear differences in survival in the presence of antigen, as opposed to the absence of antigen. The Cl-10 challenge data provided in Figures 4A and 4B, demonstrate a difference in protection due to SEQ ID NO: 28. The data provided in Figure 4A and 4B are protection models, where a mouse is first administered the antigen and then challenged with *S. aureus* CL-10. The data illustrated in Figure 4A was generated using 2.2 x 10^8 CFU/ml of CL-10, while the data illustrated in Figure 4B was generated using 2.1 x 10^8 CFU/ml of CL-10. (See the present application at page 5, lines 24-26.)

In evaluating protection against CL-10, the Office fails to consider Figure 4B. Figure 4B illustrates SEQ ID NO: 28 provides protection against *S. aureus* CL-10 going out to day 10. The Office has not argued the data in Figure 4B is not significant.

In evaluating protection against CL-10 illustrated in Figure 4A, the Office fails to take into account the ability of SEQ ID NO: 28 to delay the onset of *S. aureus* lethality. For example, no mention is made of the difference in survival rates at days 5, 6 and 7. Instead, the Office appears to only consider the day 9 and day 10 results.

With respect to CL-13 and CL-18, the Examiner's Answer makes no mention of the difference in survival rates when the mice are immunized with SEQ ID NO: 28. Figures 4C and 4D provide data showing protection from CL-13, while Figure 4F and 4G show protection

against CL-18. (The present application at page 5, lines 21-31.) In all cases, more mice survived when immunized with SEQ ID NO: 28, than when not immunized with SEQ ID NO: 28, even going out to the 10 day time point. With respect to the data shown in Figures 4F and 4G, the Office fails to present any evidence, arguments, or rationale as to why a survival rate of about 20% (about 80% death), compared to a survival rate of about 0% (about 100% death) is not significant.

C. Expectations of the Skilled Artisan Based on the SEQ ID NO: 28 Data

The Examiner's Answer points out that the skilled artisan would extrapolate data from SEQ ID NO: 28 to the corresponding ORF0657nI region from the different clinical isolates used as challenge strains:

> If one lifted or isolated the SEQ ID NO: 1-equivalent region from each sequence depicted in Figures 2A-2E and evaluated it for protection against homologous or heterologous *S. aureus* in an immune-sufficient or immune-deficient animal model, there is a **great likelihood** that one of skill in the art would observe a lack of protection as observed with fragment 2 having 91% identity to SEQ ID NO: 1, or would observe the death of approximately 80% of immunized mice upon challenge as seen with the longer polypeptide comprising an amino acid sequence that is 99.8% identical to SEQ ID NO: 1. [Bold emphasis added.]

(Examiner's Answer at page 69, lines 5-13.)

The Office position concerning the "great likelihood" of the data with longer-length SEQ ID NO: 28 being predictive of data expected from the corresponding ORF0657nI region of the challenge strain confirms Appellants' arguments concerning the relevance of such data. The Office's erroneous interpretation of the observed protection level does not take away from the importance of the experiments for predicting the ability of the corresponding ORF0657nI region from the clinical isolate to provide protection. As discussed above in Appellants Response at I.B. *supra.,* SEQ ID NO: 28 provides protection against different clinical isolates.

The Office reference to a lack of protection as observed with a fragment 2 having 91% percent identity to SEQ ID NO: 1 is not understood. None of the antigens in Figures 2A-2E have an ORF0657nI region with a sequence identity of 91% to fragment 2.

D. Office's Rebuttal Arguments on Written Description

Additional comments concerning the Office's Rebuttal are provided below. The Office's Rebuttal on pages 41 to 62 does not contain any separate sections heading. To facilitate the review of the different arguments present by the Office, Appellants have indicated the page location of the different arguments being addressed.

1. Page 42, First Paragraph

The Office asserts it has concretely established why those skilled in art would not expect a representative number of polypeptide immunogens species falling with the claims to provide protection against *S. aureus*. The assertion is indicated to be based as set forth previously and in the following sections of the Examiner's Answer.

The Office's assertion is misplaced. The Office fails to consider all the data provided in the application, mischaracterizes data provided in the application, and is based on the possibility of some unidentified alteration causing a protective polypeptide to no longer be protective.

2. Page 42, Second Paragraph

The Office indicates it does not understand Appellants reference to an amendment filed August 18, 2009. The Office correctly points out that an amendment was not filed August 18, 2009.

Appellants Appeal Brief in the section labeled f. Advisory Action Middle of Page 12 to Top of Page 13, indicated it "assumed" the Office was referring to an August 18, 2009 amendment. (Appellants Appeal Brief at page 21, fourth full paragraph.) Appellants appreciate the Office correctly pointing out that no amendment was filed on August 18, 2009. The Office's reference to additional data, in the section noted by the Appellant, may have been referring to the amendment filed August 18, 2008.

3. Paragraph going from Page 42 to Page 43

The Office indicates that contrary to Appellants remarks, page 9 of the Office Action dated November 24, 2009, does not even mention reference to von Eiff *et al.* The Office indicates that von Eiffe *et al.,* was cited with respect to claim scope.

Appellants Appeal Brief in the section labeled "g. Advisory Action Page 13 Second Full

Paragraph", indicated that it was Appellants understanding that the von Eiff *et al.* reference was previously cited to support an argument that the present polypeptides need to provide protection against homologous or heterologous strain, serotype, *Spa* type, phage type or capsular type of *S. aureus,* and cites to an Office Action dated November 24, 2009, at page 9. (Appellants Appeal Brief at page 22, lines 1-5.) The comments made in the Examiner's Answer seem to indicate that Appellants prior understanding was incorrect.

4. Paragraph going from Page 43 to Page 44

The Examiner's Answer references different descriptions in the claims and argues that contrary to Appellants' assertion, claims 33, 39, 40 and 49 are not drawn to protective polypeptides having a stronger structural relationship to polypeptides shown to be protective. The Office also provides comments with respect to "patient" provided in claims 38, 40, 42, and 44.

Appellants have argued claims 33, 39, 40, and 49 as a separate group based on reference to the immunogen having up to 25 amino acid alterations from SEQ ID NO: 1. (Appeal Brief, Argument III.C. at page 25.) Appellants' arguments included the assertion that:

> Additionally, the description of 25 alterations provides for a stronger structural relationship to polypeptides shown to be protective then the at least 94% identity. The stronger structural relationship to polypeptides such as SEQ ID NO: 1 and corresponding ORF0657nI regions illustrated in the application, provides additional support for the polypeptides being representative of the genus.

(Appellants Appeal Brief at page 25, fourth paragraph.)

The application illustrates the ability of the ORF0657nI region of SEQ ID NO: 1 to provide protective immunity, and includes heterologous protection data based on SEQ ID NO: 28. Referencing up to 25 amino acid alterations provides for a stronger structural relationship to SEQ ID NO: 1, than referencing having at least a 94% identity to SEQ ID NO: 1.

With respect to a human "patient" the Office indicates that:

> The limitation 'patient is a human' in claims 38, 40, 42 and 44 does not exclude, but includes immune-sufficient, immune-deficient, immunocomprised, and imunosuppressed human patients, including cancer patients, AIDS patients, patients with organ transplantation, and patients with end-stage kidney disease etc., among whom multiple drug-resistant and vancomycin-resistant *S. aureus* infections are known to cause increased mortality and morbidity. The limitation 'patient is a human' also includes neonates, infants, pediatric and geriatric patients as well.

(Examiner's Answer at page 44, lines 7-14.)

The Office description of patient appears to be a new one, in that the provided list is a longer than previously cited by the Office. The Office now appears to be providing an argument directed to providing protection against every *S. aureus* organism in all hosts.

In response to similar arguments, but with a significantly narrower range of "humans", Appellants have pointed out:

> The patent office is improperly rejecting the claims based on arguments requiring the immunogens to provide protection against every possible *S. aureus* in a non-human or human host, and for claims referencing a patient requiring the immunogen to be effective against immunosufficient, immunodeficient and immunocompromised patients. Such arguments are directed to how a particular polypeptide is used and not whether written description is provided for the claimed immunogen.

(Response filed February 24, 2010 at page 12, fourth paragraph.)

The Office responded by arguing:

> The Office has previously set forth sufficient rationale and has established a clear lack of written description. Contrary to Applicants' assertion, no requirements were made for illustration of the ability of the claimed polypeptide to provide protective immunity against each and every *S. aureus* in a non-human or human host, including immunosufficient, immunodeficient and immunocompromised patients. Instead, the Office action analysed and set forth the scope of the claims under 25 U.S.C 112, first paragraph as required. The reference of von Eiff *et al.* was properly cited to document the existence immunologically heterogeneous or distinct types among *Staphylococcus aureus.*

(Advisory Action dated March 25, 2010, at page 13, first full paragraph.)

The Office's new reference to additional patients having weakened immune systems appears to be an effort to find a patient unable to mount an immune response when vaccinated. The claims in question are directed to immunogens and pharmaceutical compositions. How a particular immunogen is used goes to enablement of a method of use. Given the examples

provided in the application using animal models, additional effectiveness in a non-human or human (e.g., immunodeficient, immunosuppressed and immunocompromised patient) does not need to be shown.

5. Paragraph going from Page 44 to Page 45

The Examiner's Answer presents arguments that reference to "immunogen" in claim 7 indicates protective immunity. The Office also asserts "Appellants' current argument that the immunogen of claim 7 is not associated with the protective function is contrary to the express definition provided in the as-filed specification." (Examiner's Answer at page 45, last line to page 46, line 2.) The Office does not refer to any particular argument presented by the Appellants.

Appellants Appeal Brief in the section entitled "F. The Data and Guidance in the Application Provides Written Description Support for Claim 7" provides arguments concerning the ability of immunogens covered by claim 7 to provide protection. (Appellants Appeal Brief at page 28, lines 1-7.) For example, Appellants Appeal Brief points out "[t]he heterologous protection data provided in the application illustrates that alterations could be made to SEQ ID NO: 1 and the resulting polypeptide would be protective." (Appellants Appeal Brief at page 28, lines 1-2.) Appellants Appeal Brief also points out that a fragment not protective is functionally excluded from the claims. (Appellants Appeal Brief on page 28, lines 3-7.)

6. Paragraph going from Page 46 to Page 47

The Examiner's Answer asserts:

> Contrary to Appellants' arguments, the scope of the instantly claimed genus is not limited to a single polypeptide or immunogen species consisting of an amino acid sequence 100% identical to SEQ ID NO: 1 with no amino acid alterations therein, or to a 99.8% identical variant species containing a single amino acid alteration exclusively after the N-terminal methionine of SEQ ID NO: 1.

(Examiner's Answer at page 46, lines 3-8.) The Office goes on to indicate the claims encompass a broader scope. The Examiner's Answer does not reference any particular claim with respect to claim scope, and does not indicate where the Appellants made such arguments.

Appellants Appeal Brief concerning written description divided the claims into different groups based on sequence identity or the number of amino acid alterations. (Appellants Appeal

Brief on page 9, third paragraph.) Appellants have not argued that the claims allowing for a referenced sequence identity or number of alteration are limited to an amino acid sequence 100% identical to SEQ ID NO: 1 with no amino acid alterations therein, or to a 99.8% identical variant species containing a single amino acid alteration exclusively after the N-terminal methionine of SEQ ID NO: 1.

7. Page 47, first full Paragraph, and Paragraph going from Page 47 to 48

The Examiner's Answer indicates that the percent identity of the claims is relative to SEQ ID NO: 1, not SEQ ID NO: 2 or SEQ ID NO: 28. The Examiner's Answer also indicates that SEQ ID NO: 2 is not covered by the claims.

8. Page 48, first full paragraph

The Examiner's Answer argues that Appellants were not in possession of *S. aureus* strains containing naturally occurring ORF0657nI or ORF0657nH regions; the state of the art does not document the existence of such strains; and without the knowledge whether ORF0657nI or ORF0657nH is buried in the cell wall it would not be predictable whether naturally occurring ORF0657nI or ORF0657nH are protective.

The Office's arguments fail to take into account the teaching and guidance provided in the present application. The present application provides data demonstrating polypeptides corresponding to ORF657nI and ORF0657nH regions are sufficient to generate a protective immune response. Such data demonstrates that the target polypeptide is accessible to an immune response generated with polypeptides providing ORF657nI or ORF0657nH regions. (See, for example, the present application Examples 3 and 16 and accompanying figures.)

The present application provides different examples of naturally occurring ORF0657nI and ORF0657nH sequences. See, for example, Figures 2A-2E providing ORF0657nH regions encompassing ORF0657nI, and page 13, lines 2-13 providing ORF0657nI related regions.

9. Paragraph going from Page 48 to Page 50

The Office notes that certain sequences are not covered by the claims including SEQ ID NOs: 2 and 28. The Office concludes the paragraph by asserting:

> Furthermore, the ORF0657nI-equivalent region of SEQ ID NO: 2 or SEQ ID NO: 28 does not constitute a 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99.0% identical variant species of an amino acid sequence consisting of SEQ ID NO: 1, when sequence identity is determined using an art-recognized algorithm. Therefore, SEQ ID NO: 28 and SEQ ID NO: 2 do not fall within the scope of the instant claims.

(Examiner's Answer at page 50, lines 4-10).

As discussed in Appellants Response at I.C. *supra.,* the Office position concerning the "great likelihood" of the data with longer-length SEQ ID NO: 28 being predictive of data expected from the corresponding ORF0657nI region of the challenge strain confirms Appellants arguments concerning the relevance of such data. The Office's erroneous interpretation of the level of protection, does not take away from the importance of the observed protection in predicting the ability of the corresponding ORF0657nI region from the clinical isolate to provide protection.

Thus, even though SEQ ID NO: 2 and SEQ ID NO: 28 are not covered by the existing claims, the protection data generated with SEQ ID NO: 28 along with other data provided in the application reasonable coveys to the skilled artisan that Applicants were in possession of the claimed genus. Such data demonstrates that SEQ ID NO: 1 is representative of the claimed species and that the prophetic examples of different ORF0657nI regions described in the application would also be protective. (See, Appellant Response I.A., I.B., and I.C. *supra*., and Appellants Appeal Brief Argument I. at pages 8-16.)

Appellants do not understand the Office's reference to ORF0657nI-equivalent region and art-recognized algorithm, or the Office's reference to "[f]urthermore as Appellants have acknowledged previously, the ORF0657nI region of SEQ ID NO: 1 that overlaps with a portion of SEQ ID NO: 28 is 78% of SEQ ID NO:28. See second paragraph on page 11 of Appellants' amendment remarks filed 02/24/2010." (Examiner's Answer, at page 49, lines 13-15.)

In the response filed 02/24/2010 Appellants pointed out the significant overlap between the region of ORF0657n left after cellular processing and the ORF0657nI region:

> The ORF0657nI region of SEQ ID NO: 1 also has a significant overlap with the portion of SEQ ID NO: 28 remaining after cellular processing. The overlap contains an exact match of 445 amino acids out of 572. The overlap runs across about 78% of the relevant portion of SEQ ID NO: 28. Example 3, discussed above, illustrates that the ORF0657nI region is sufficient to provide protective immunity.

(Response filed 02/24/2010, at page 11, second paragraph.)

The significant overlap between ORF0657nI and the region expected to be attached to the cell wall further support Appellants arguments concerning the teaching provided by the heterologous protection data. The teaching provided by the data include demonstrating the ORF0657nI region is sufficient to generate a protective immune response against the heterologous *S. aureus* challenge strain Becker, and the ability of SEQ ID NO: 28 to provide protection against additional heterologous strains supports the scope of the claims. (See, Appellant Response I.A., I.B., and I.C. *supra*., and Appellants Brief Argument I. at pages 8-16.)

10. Paragraph going from Page 50 to Page 51

The Examiner's Answer provides comments concerning SEQ ID NO: 3, 4, and 5. SEQ ID NO: 5 is noted to be a species consisting of an amino acid sequence 99.8% identical to SEQ ID NO: 1. SEQ ID NO: 4 is characterized as a polypeptide consisting of an amino acid sequence 99.8% identical to SEQ ID NO: 1 plus additional amino acids. SEQ ID NO: 3 is indicated to be representative of a species containing SEQ ID NO: 1 and well over 20 additional amino acid at the carboxy terminus.

No mention is made concerning Appellants' pointing out that the polypeptides were used in heterologous experiments and the skilled artisan would expect the corresponding region from the challenge strain to also provide protection. The Office fails to provide a rationale as to why the corresponding region would not provide similar protection, and as discussed in Appellants Brief at I.C. *supra.,* the Office takes the position that data with SEQ ID NO: 28 is relevant in evaluating expectations for the corresponding ORF0657nI region from the challenge strain.

11. Paragraph going from Page 51 to Page 52

The Examiner's Answer argues the ability of SEQ ID NOs: 4 and 5 to provide "moderate" protection demonstrates that it is "critical" for the claimed sequence to have at least 99.8% sequence identity and not have a single amino acid alteration along the length of SEQ ID NO: 1, except the N-terminal amino acid addition and the first methionine. Protection data with SEQ ID NO: 3 is indicated to support a SEQ ID NO: 1 region having more than 20 amino acid moieties at the carboxyl terminus. The Office also argues SEQ ID NO: 4 did not provide statistically significant protection, and refer to the alleged consistent non-reproducible protection being

discussed in the subsequent section of the Examiner's Answer that highlights the issue of unpredictability.

The Office fails to address the heterologous nature of the experiments and also fails to provide any rationale or evidence as to why protection with a particular polypeptide is evidence that every single, or a significant percent, of the amino acids present in a protective polypeptide are "critical" for protection. The heterologous protection data provides evidence that amino acids can be varied.

The Office continues to argue that Figure 3B data with SEQ ID NO: 4 did not provide statistically significant protection. The Office fails to indicate any particular criteria as to what was considered in concluding no statistically significant protection. For example, is the Office referring to protection at day 3, day 10, or some other day? Figure 3B at days 3 and 4 provides for a greater difference in survival between animals receiving SEQ ID NO: 28 than the control, indicating at a minimum a significant difference in delaying onset of *S. aureus* lethality attributed to SEQ ID NO: 28.

The Office also fails to consider other data provided in the application in evaluating SEQ ID NO: 4, such as data provided in Figure 10 or Figure 3C. Figure 10 illustrates that SEQ ID NO: 4 is protective.

The Office characterizes the data for SEQ ID NO: 4 in Figure 10 as providing "moderate" protection. Appellants appreciate the Office acknowledging protection was obtained. As to the degree of protection, the Office fails to define what is meant by "moderate" protection as opposed to a high level of protection.

Figure 3C illustrates that SEQ ID NO: 5 is protective. SEQ ID NO: 4 corresponds to the ORF0657nH region and SEQ ID NO: 5 corresponds to the ORF0657nI region. The Office appears to be taking the position that the data with the shorter ORF0657nI is sufficient to provide protection, while the longer fragment is not. No rationale is provided by the Office for such a distinction.

12. Paragraph going to page 53 to 54

The Examiner's Answer indicates whether SEQ ID NO: 1 is protective is not the issue. The Office argues that SEQ ID NO: 1 is not sufficiently representative of the claimed species.

The Office's position fails to take into account that protection provided by SEQ ID NO: 1 demonstrates that ORF0657nI is sufficient to provide protection against a heterologous strain Becker challenge, and the data generated with SEQ ID NO: 28 against different clinical isolates of *S. aureus*. The use of SEQ ID NO: 28 to provide protection against different heterologous strains provides further evidence that SEQ ID NO: 1 is representative of the claimed species and that the skilled artisan would expect that sequences provided by prophetic examples would also be protective. (See, for example, Appellants Response at I.A., I.B. and I.C. *supra.*)

13. Paragraph going from to page 54 to Page 55

The Examiner's Answer refers to Figure 1A and indicates it has assumed that the SEQ ID NO: 1 indication of protection is at least a moderate level of protection as seen in Figure 10 for SEQ ID NO: 5, and not similar to the protection represented by Figures 4A, 4D, and 4G for SEQ ID NO: 28, or Figure 3B for SEQ ID NO: 4. The Office also indicates that Appellants were incorrect in alleging data illustrating the ability of SEQ ID NO: 1 to provide protection were not considered.

The Office assumption concerning protection indicated in Figure 1A and its comments on Figures 4A, 4D, and 4G for SEQ ID NO: 28 are new arguments. The indication of protection illustrated in Figure 1A is based on data provided in the application. (See, Figure 3A, 3B, 3C, and Figure 10.)

The Office comments concerning the degree of protection provided by SEQ ID NO: 4 fails to take into account the data provided in the application. Figure 10 illustrates that SEQ ID NO: 4 is protective going out to 10 days, Figure 3B illustrates protection by showing a delay in lethality induced by SEQ ID NO: 4, and Figure 3C illustrates protection using a shorter-length SEQ ID NO: 5. The Office fails to indicate the criteria used to conclude Figure 3B does not provide protection; and indicates that data in Figure 10 using SEQ ID NO: 4 shows protection. (See, Appellants Response I.D.11., *supra.*)

The Office comments concerning the degree of protection provided Figures 4A, 4D, and 4G incorrectly attribute cell death to the antigen, and fails to consider the difference in survival attributed to the antigen. (See Appellants Response I.B. *supra.*)

14. Paragraph going from Page 55 to Page 56

The Examiner's Answer refers to Appellants arguments concerning the amino acid 82-486 fragment being on the outer limits of claim 7 and the percent identity argument provided with respect to Figures 2A-2E. The Office indicates that the percent identity argument fails to align each of the individual ORF065nI sequences and compare it to SEQ ID NO: 1 using an art-accepted algorithm.

Appellants' calculation of differences was intended to illustrate the present application provides examples of particular amino acid positions varying from strain to strain. The differences between the strains are variable regions that would not be expected to be critical for protection. The expectation of protection is supported using SEQ ID NO: 28 and representative challenge clinical isolates CL-10, CL-13, CL-30, CL-18 and CL 21. (See Example 6 of the application and Figures 4A-4H.) These clinical isolates are diverse *S. aureus* strains with different degrees of sequence identity to the ORF0657nI region of SEQ ID NO: 1.

The Office fails to consider the importance of the different variable regions in reasonably conveying to one skilled in the art that Appellants possessed the genus of a protective immunogen having at least 90% identity to the SEQ ID NO: 1. As described in Appellants Appeal Brief, consideration of the different variable regions in the ORF0657nI region identifies 49 alterations that provide for a sequence identity of 89%. (Appellants Appeal Brief Argument I.F., at pages 27-28.) Rather than consider the substance of the Appellant Response, the Office agues the absence of an art-accepted algorithm that takes into account variable regions from different strains.

15. Paragraph going from page 56 to page 58

The Examiner's Answer provides several comments on the amino acid sequences disclosed in Figures 2A-2E. The Office notes that the percent identity in the instant claims is relative to SEQ ID NO: 1; CL-10, CL-13, CL-30, and CL-21 depicted in Figure 2 are full-length sequences not sequences consisting of an amino acid sequence 94% identical to SEQ ID NO: 1; and SEQ ID NO: 2 is excluded from the claims.

With regard to Appellants reference to protection data with SEQ ID NO: 28 the Office asserts:

> Contrary to Appellants' assertion, SEQ ID NO: 11 (CL-10); SEQ ID NO: 18 (CL-18); SEQ ID NO: 19 (CL-13); SEQ ID NO: 22 (CL-21); and SEQ ID NO: 24 (CL-30) having up to 22 alterations in the non-N-terminal ORF0657nI regions do not and cannot provide evidence of possession at the time of filing, since the ORF0657nI regions of these full-length sequences have not been correlated with the requisite function, i.e., homologous or heterologous protection, with or without an adjuvant, in an immune-sufficient animal subject, let alone a human or non-human patient, including an immune-deficient or an immunocompromised patient or non-human patient.

(Examiner's Answer at page 57, lines 14-23.) The Office concludes by asserting:

> In sum, the protection conferred by an amino acid sequence consisting of SEQ ID NO: 1 or an amino acid sequence differing from SEQ ID NO: 1 by a single amino acid addition after the N-terminal methionine cannot be extrapolated to SEQ ID NO: 11 (CL-10); SEQ ID NO: 18 (CL-18); SEQ ID NO: 19 (CL-13); SEQ ID NO: 22 (CL-21), and SEQ ID NO: 24 (CL-30), because these sequence comprise multiple amino acid alterations along the non-amino terminal parts of the ORF0657nI-equivalent region.

(Examiner's Answer at page 58, lines 4-11.)

The Office's comments ignore the importance of the ORF0657nI region present in the SEQ ID NO: 28 and the teachings provided in the application. As further discussed above the application identifies the ORF0657nI region as sufficient to generate an immune response; and the protection data with SEQ ID NO: 28 against the heterologous strains CL-10, CL-13, CL-30, CL-18 and CL-21 further supports SEQ ID NO: 1 being representative of the claimed genus, provides support for additional representative species described in the application being protective, and confirms the expectation that alterations can be made to a SEQ ID NO: 1 where the resulting polypeptide retains its protective ability. (Appellant Response I.A., I.B., and I.C. *supra*.)

16. Paragraph going from page 58 to page 59

The Examiner's Answer indicates that contrary to Appellants assertion, the naturally occurring strain Becker sequence present in *S. aureus* is not covered by the instant claims. The Office goes on to indicate that at the time the application was filed applicants were not in possession of the Becker ORF0657n sequence providing protection, the Becker sequence was not part of the filed application, the 95% identity to the Becker sequence in Table 3 is with respect to SEQ ID NO: 2, and there is no evidence in the application as filed that native or

altered COL sequence variants falling within the scope of the claims were tested against a homologous strain.

Appellants have not argued the full-length naturally occurring ORF0657n sequence present in strain Becker is covered by the instant claims. The sequence comparison provided Appellants Appeal Brief, Appendix B, identifies 17 amino acid differences between SEQ ID NO: 1 and the corresponding region from Strain Becker. The 17 amino acid differences provides a sequence identity of about 96% (446-16/446 x 100), for the ORF0657nI region. (See the present application at page 8, lines 12-15 for the formula calculating sequence identity.) Thus, the ORF0657nI region of the strain Becker sequence is covered by the claims referencing at least 94% sequence identity to SEQ ID NO: 1.

Table 3, of the present application, indicates the sequence identity to strain Becker across the SEQ ID NO: 2 region. (The present application at page 29.) Clearly, Applicants were in possession of the strain Becker sequence when the application was filed. To determine sequence identity, the sequences must be known.

The present application identifies strain Becker as the challenge strain for the experiments of Example 3, illustrated by Figure 3A, 3B and 3C. (See the present application on page 5, lines 22.) The data with His-tagged SEQ ID NO: 5 illustrates that SEQ ID NO: 1 is sufficient to generate a protective immune response against strain Becker. (The present application at Figure 3C). SEQ ID NO: 5 differs from SEQ ID NO: 1 by replacing the amino terminus methionine with methionine-glycine. (See Figure 2A-2E of the present application).

Given the ability of SEQ ID NO: 5 to provide protection against strain Becker, the skilled would expect the strain Becker ORF0657nI sequence to provide protection at least against strain Becker. As further discussed in Appellants Appeal Brief, such an expectation is based on a homologous challenge involving the use of a polypeptide immunogen having the same region as the challenge strain, where in a heterologous challenge the sequence used to induce the immune response is different from that actually present. (See, Appellants Appeal Brief Argument I.A.2. on pages 12-13.)

While the strain Becker sequence is not shown in the application, based on random chance, one of ordinary skill in art would expect amino acid differences between *S. aureus* strain Becker and COL to be located in different regions including the ORF0657nI. Figures 2A-2E of the present application support such an expectation by providing evidence that differences

among different ORF0657n sequences occur in different locations including the OFR0657nI region. The sequence comparison between the strain Becker ORF0657n, SEQ ID NO: 1, SEQ ID NO: 3, SEQ ID NO: 4 and SEQ ID NO: 5 provided in Appellants Appeal Brief confirms the evidence provided in the application, and what would be expected by one skilled in the art, concerning the presence of different alterations between COL and Becker being located in different regions, including the ORF0657nI region. (See, Appellants Appeal Brief Argument I.A.2. at pages 12 to 13, and Appellants Appeal Brief Exhibit B.)

It is not clear what is intended by the Office's comments on Appellants not testing for homologous protection using COL. If the intention is to argue that homologous protection is not predictable in light of the heterologous protection, such an argument fails to consider the information conveyed by the heterologous protection data.

Based on the ability of SEQ ID NO: 5 to protect against strain Becker, the skilled artisan would also expect SEQ ID NO: 5 to provide protection against *S. aureus* COL. The ORF0657nI region of SEQ ID NO: 5 is based on the COL sequence. Using SEQ ID NO: 5 against COL would be a homologous challenge experiment. Given that SEQ ID NO: 5 induced protection against the heterologous strain Becker, it would be expected to produce protection against COL. Such an expectation is based on a homologous challenge involving the use of a polypeptide immunogen having the same region as the challenge strain, where in a heterologous challenge the sequence used to induce the immune response is different from the targeted polypeptide present in *S. aureus*.

17. Paragraph going from page 59 to page 60

The Examiner's Answer argues the present application fails to identify any protective B-cell or T-cell epitopes and SEQ ID NO: 28 induces death of approximately 80% mice. The Office concludes the rejection is supported by SEQ ID NO: 28 data provided in Applicants specification and are not Office speculations.

The use of longer-length SEQ ID NO: 28 to provide protection against different strains of *S. aureus* provides evidence that SEQ ID NO: 1 is representative of the claimed species and that the skilled artisan would expect that sequences provided by prophetic examples would also be protective. (See, for example, Appellants Response I.A., I.B., and I.C. *supra.*)

As more fully discussed above in Appellants Response I.B. *supra*, the Office's comments

concerning SEQ ID NO: 28 inducing cell death are incorrect. Cell death is caused by the *S. aureus* challenge strain, not SEQ ID NO: 28. The SEQ ID NO: 28 data provided in the application illustrates enhanced survival due to SEQ ID NO: 28.

18. Paragraph going from page 60 to the end of page 61

The Examiner's Answer asserts the Office has "clearly" established a *prima facie* case of a lack of written description, and argues that Appellants have not shown a sufficient number of varied species or structure function to support the claimed genus. The Office refers to art-recognized unpredictability associated with amino acid alterations and Appellant-demonstrated unpredictability.

Appellants disagree with the assertion concerning the establishment of a *prima facie* case of a lack of written description. Absent from the Office's *prima facie* case, is consideration of the degree of predictability for the different claims based on the data provided in the present application. As discussed in Appellants Response I.A., IB., and I.C. *supra.,* the Office fails to consider all the data, and erroneously asserts that SEQ ID NO: 28 induces cell death.

The Office also fails to address the degree of predictability for claims having different scope. Appellants Appeal Brief argued different groups of claims based on the structural relationship to SEQ ID NO: 1. The different groups were: (A) claims 1, 8, 9, and 38; (B) claim 4; (C) claims 33, 39, 40, and 49; (D) claims 34, 41, 42, and 50; (E) claims 35, 43, 44, and 51; and (F) claim 7. (Appellants Appeal Brief Argument I. at page 9, third paragraph.)

Group A (claims 1, 8, 9 and 39) includes a description of a polypeptide immunogen with an amino acid sequence at least 94% identical to SEQ ID NO: 3 or a fragment of said amino acid sequence comprising a sequence at least 94% identical to SEQ ID NO: 1. In arguing for a *prima facie* case of no written description the Office focused on the limitation of at least 94% identical to SEQ ID NO: 1. (Appellants Appeal Brief Argument I.A.)

The Office ignored the high degree of structural relationship between members of the genus provided by 94% identity in asserting the species is widely variant. The Office also ignored the heterologous protection data provided in the application, and fails to provide a rationale as why a significant number of polypeptides within the claimed genus would not be expected to retain the ability to provide protective immunity in evaluating predictability. (Appellants Appeal Brief Argument I.A.)

Group B (claim 4) further describes the polypeptide immunogen of claim 1 by indicating the immunogen consists of an amino acid sequence at least 94% identical to SEQ ID NO: 1, SEQ ID NO: 3 or SEQ ID NO: 42. The rejection appears to be based on reference to at least 94% identical to SEQ ID NO: 1. As with the Group A, the Office ignores the high degree of structural relationship between member of the genus provided by 94% identity, ignores the heterologous protection data provided in the application, and fails to indicate why a significant number of polypeptides within the claimed genus would not be expected to retain the ability to provide protective immunity. (Appellants Appeal Brief Argument I.B.)

Group C (claims 33, 39, 40, and 49) further describe the polypeptide immunogen by indicating the immunogen has up to 25 amino acid alterations from SEQ ID NO: 1. SEQ ID NO: 1 has 446 amino acids. The Office ignores the high degree of structural relationship between members of the genus provided by the description of up to 25 amino acid alterations, ignores the heterologous protection data provided in the application, and fails to indicate why a significant number of polypeptides within the claimed genus would not be expected to retain the ability to provide protective immunity. (Appellants Appeal Brief Argument I.C.)

Group D (claims 34, 41, 42, and 50) further describes the polypeptide immunogen by providing for up to 10 amino acid alterations from SEQ ID NO: 1. The Office ignores the high degree of structural relationship between members of the genus provided by the description of up to 10 amino acid alterations, ignores the heterologous protection data provided in the application, and fails to indicate why a significant number of polypeptides within the claimed genus would not be expected to retain the ability to provide protective immunity. (Appellants Appeal Brief Argument I.D.)

Group E (claims 35, 43, 44, and 51) further describe the polypeptide immunogen by providing for up to 5 amino acid alterations from SEQ ID NO: 1. The Office ignores the high degree of structural relationship between members of the genus providing by the description of up to 5 amino acid alterations, ignores the heterologous protection data provided in the application, and fails to indicate why a significant number of polypeptides within the claimed genus would not be expected to retain the ability to provide protective immunity. (Appellants Appeal Brief Argument I.E.)

Group F (claim 7) is directed to an immunogen consisting of an amino acid sequence at least 90% identical to SEQ ID NO: 1 and one or more additional regions or moieties covalently

joined to the sequence at the carboxyl terminus or the amino terminus. In this case, the Office cites to the application indicating that a species within the genus is not protective (amino acids 82-486). It is respectfully submitted the Office improperly ignores Appellants' argument concerning the number of alterations that could be obtained by combining the different ORF0657nI regions provided in the application. (Appellants Appeal Brief Argument I.F.)

19. Page 62-67

The Examiner's Answer alleges that Appellants themselves provided an abundance of evidence to justify the rejections. The Office goes on to reference four Evidence numbers.

a. Evidence Number 1

The Examiner's Answer refers to the patent application indicating that fragments of SEQ ID NO: 2 that provided amino acids 82-486 and 42-196 were not protective. The Office notes the 82-486 fragment has as high as 91% identity to SEQ ID NO: 1 and falls within claim 7. The Office indicates that splitting an active fragment into two inactive pieces raises the possibility of potential conformation protective epitopes, and argues this showing points to the criticality of retaining all amino acid residues.

Assuming conformational epitomes are present, the Office is incorrect in extrapolating that it is critical to retain all the amino acids of SEQ ID NO: 1 except the N-terminal methionine. No basis for the necessity of retaining every single amino acid of SEQ ID NO: 1 is provided.

As discussed above, heterologous data protection provided in the application clearly demonstrates that changes could be made to SEQ ID NO: 1 and still retain function. (See Appellants Response I.A., I.B., and I.C. *supra.*)

To the extent that the 82-486 fragment is not protective, such a fragment is excluded from claim 7. The other pending claims provide for 94% or greater identity, and do not encompass the 82-486 fragment. In addition, to the extent that the 82-486 fragment is not protective, the application provides guidance that N-terminal 40 amino acids from SEQ ID NO: 1 should not be removed.

b. Evidence Number 2

The Office refers to protection data provided in Figure 3B concerning SEQ ID NO: 4, and argues that such a species "cannot and would not" be considered by those skilled in art as protective. (Examiner's Answer at page 65, lines 20-23.) The Office indicates the SEQ ID NO: 4 polypeptide provides almost the same level of survival as induced in the control mice.

The Examiner's Answer fails to consider the different data in the application providing evidence that SEQ ID NO: 4 is protective. Figure 10 illustrates that SEQ ID NO: 4 is protective, Figure 3B illustrates protection by showing a delay in lethality induced by SEQ ID NO: 4, and Figure 3C illustrates protection using a shorter-length SEQ ID NO: 5. The Office fails to indicate the criteria used to conclude Figure 3B does not provide protection, fails to provide a rationale for the skilled artisan not considering the SEQ ID NO: 5 being protective in evaluating SEQ ID NO: 4, and ignores its own assertion that SEQ ID NO: 4 shows protection. (See Appellants Response Section I.D.11 *supra*.)

c. Evidence number 3

The Examiner's Answer argues that SEQ ID NO: 28 induces cell death in clinical isolates. SEQ ID NO: 28 does not induce cell death. Cell death is induced by *S. aureus*. Consideration of the difference in survival rates between SEQ ID NO: 28 vaccinated animals and animals only obtaining AHP adjuvant demonstrates SEQ ID NO: 28 is causing an increase in survival. (Appellants Response I.B. *supra*.)

d. Evidence number 4

The Examiner's Answer refers to additional data provided in an amendment filed 08/18/2008, and argues the "[a]ppellants' additional data made of record and the data from the specification concretely establish that the polypeptide immunogen species falling within the scope of the claims were protective in one host species only when administered with AHP or the endotoxin adjuvant." (Examiner's Answer at page 66, line 24 to page 67, line 2.) The Office also argues that if the additional data was extrapolated to a human patient, including immunosufficient, immunodeficient, immunosuppressed, and immunocompromised human, even the ORF0657nI corresponding sequence would be expected to be non-protective in human patients without an adjuvant.

The Office fails to properly consider all of the data provided in the application and the additional data provided in the August 18, 2008 amendment. Consideration of all the data supports the scope of the pending claims.

The data provided in the application demonstrates the ORF0657nI region induces a protective immune response. (See, Appellants Response I.A., I.B., and I.C. *supra.*) AHP is an aluminum hydroxyphosphate adjuvant. (See, the present application at page 26, lines 22-23.) AHP does not contain polypeptides from *S. aureus* and the immune response is not directed against AHP. The data provided in the application illustrates an increase in survival attributed to the antigen.

The additional data for ORF0657nI indicated that endotoxin has an adjuvant effect in the BALB/C mice model. The additional data also indicated that yeast produced ORF0657nI not containing endotoxin provided protective immunity in ICR mice. The data indicates variability in the employed animal model for the ORF0657nI antigen, and a protective immune response for an ORF0657nI antigen could be produced in the absence of endotoxin.

The Office's comment concerning extrapolating the data to use in humans requiring an adjuvant is clearly not supported. The experiments described in the application do not indicate the extent to which AHP can be used to enhance the immune response of ORF0657nI. Experiments performed to determine the additional benefit of AHP for ORF0657nI would need a control where ORF0657nI was provided without any AHP. The application does not provide data for such an experiment.

20. Conclusion (Pages 67-70)

The Examiner's Answer concludes by summarizing different allegations. The different allegations either mischaracterize the data provided in the application or fail to consider all of the data.

In summarizing the different allegations, the Examiner's Answer refers to ORF0657nI fragment 2, protection data in Figure 3B, the additional data concerning endotoxin, and the 80% "death" induced by SEQ ID NO: 28. The Office attempts to pull together the different pieces of alleged evidence:

> In other words, a showing that an amino acid sequence 99.8% identical to SEQ ID NO: 1, which when comprised within the longer sequence of SEQ ID NO: 28 (a) kills approximately 80% of immunesufficient mice immunized with SEQ ID NO: 28 admixed with the AHP adjuvant following challenge infection with the CL-10, CL-13, or CL-18 clinical isolate of *S. aureus*; and (b) provides almost the same degree of mortality as induced in the control mice by AHP adjuvant alone against CL-10 isolate of *S. aureus*; or (c) provides a moderate protection of approximately 40% against a laboratory strain *S. aureus* compared to the 20% protection conferred by AHP adjuvant alone, is insufficient to show possession of the huge genus of polypeptide variants or immunogen variants of the recited percent sequence identity as claimed.

(Examiner's Answer at page 68, lines 8-19)

Appellants have provided responses throughout Appellants Reply Brief to the different allegations, which are summarized below:

(a) The alleged death rate of 80% is based on a fundamental misunderstanding of the data. SEQ ID NO: 28 does not induce death. *S. aureus* induces death. The Office provides no rationale as to why 20% survival for vaccinated animals would not be significant given the unvaccinated animals have a significantly less survival. The data with SEQ ID NO: 28 illustrates protection which supports the pending claims. (See, Appellant Response I.A., I.B., and I.C. *supra.*)

(b) The Office's reference to data for CL-10 (Figure 4A) fails to consider the greater degree of protection provided by SEQ ID NO: 28 at, for example, days 5 and 6; and the data for CL-10 provided in Figure 4B. (See, Appellant Response I.B. *supra.*)

(c) The Office's reference to moderate protection of 40% compared to 20% protection conferred by AHP alone, does not indicate the basis or importance of characterizing the protection as moderate. Appellants appreciate the Office conceding protection was obtained, and that more protection was obtained in the absence of AHP. As discussed in Appellant Response I.A., I.B., and I.C. *supra.*, the application provides additional protection data with SEQ ID NO: 28, which was erroneously argued by Office as inducing cell death.

(d) The protection data with ORF0657nI fragment 2 concerns a polypeptide that has about 91% identity to SEQ ID NO: 1. such a fragment is functionally excluded from Claim 7 and the other claims provide for a sequence identity that would not encompass the fragment. Appellants provide additional arguments supporting the at least 90% sequence identity in claim

7, based on variable amino acid positions present in different clinical isolate. The substance of such arguments were not considered by the Office. (See, Appellant Response I.D.14. *supra*.)

(e) The Office's conclusion alleging the inability of SEQ ID NO: 4 to provide protection fails to explain the criteria used in coming up with the conclusion and fails to take into account the data provided in the application. Figure 10 illustrates that SEQ ID NO: 4 is protective, Figure 3B shows protection by illustrating a delay in lethality induced by SEQ ID NO: 4, and Figure 3C illustrates protection using a shorter-length SEQ ID NO: 5. (See, Appellants Response I.D.13 *supra*.); and

(f) The additional data concerning endotoxin and ORF0657nI, also includes data illustrating protection in ICR mice in the absence of endotoxin when ORF0657nI was used. (See, Appellants Response I.D.19.d. *supra*.)

II. Claim 7 Complies with 35 U.S.C. § 112, Second Paragraph (Definiteness)

The Office indicates it is unclear in claim 7 the stability of which polypeptide is facilitated by the one or more additional regions or moieties. The Office's position appears to be that claim 7 does not indicate a purified polypeptide, and in those circumstances when other polypeptides are present it is not clear the stability of which polypeptide is enhanced.

Claim 7 indicates the additional region or moiety is joined to an immunogen comprising an amino acid sequence at least 90% identical to SEQ ID NO: 1. Reference to amino acid sequence provides for a polypeptide. The skilled artisan reading claim 7 would readily understand the additional region or moiety facilitates stability of the polypeptide it is attached to, which is the only amino acid sequence specifically recited as present. Definiteness under 35 U.S.C. 112, second paragraph, is determined based on whether "those skilled in the art would understand what is claimed when the claim is read in light of the specification." *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986).

III. Claim 8 Complies with 35 U.S.C. § 112, Second Paragraph (Definiteness)

The Examiner's Answer continues to argue that claim 8 is indefinite based on reference to "provides protective immunity against *S. aureus*" in line 3, while the earlier part of the claim refers to inducing a protective immune response in a patient. According to the Office, the claim encompasses an immunologically effective amount of a purified immunogen that provides

protective immunity in a non-patient or a patient other than recited in line 2. (Examiner's Response at page 72, line 23 to page 74, line 1.)

As discussed in Appellants Appeal brief, the preamble description of a patient indicates a possible use of the composition. Reference to providing protective immunity against *S. aureus* in the body of the claim refers to a property of the composition consistent with the claim preamble. (Appellants Appeal Brief Argument II.) The skilled artisan reviewing claim and the specification would readily understand that when the composition is used, the production of an immune response is to occur in the patient to which the immunogen is administered.

IV. Claims Depending upon Claims 7 and 8

Claims 9 and 38-54, which depend directly or indirectly from claims 7 or 8, are rejected as allegedly indefinite. The rejection is based on claims 7 and 8 allegedly being indefinite. As discussed above, claim 7 and 8 are not indefinite. (Appellants Response II. and III. *supra*.) Appellants note that claims dependent upon claim 7 were argued in a different group from claims dependent upon claim 8.

V. Claims 5 and 6 Stand Objected as Covering a Non-Elected and Non-Searched Species

The Office indicated that claims 5 and 6 cover non-elected species and that a search and further consideration of the non-elected species is needed. (Advisory Action dated 3/25/2010, at page 17, under Remarks.) Claims 5 and 6 refer to SEQ ID NO: 1, 3, 7, 17, 20, or 42.

The provided objection appears to be based on the argument that the generic description covering the non-elected species is allegedly not patentable. As discussed in Argument I. *supra.*, claim 1 is allowable. The percent identity polypeptide description provided in claim 1 covers the polypeptides species listed in claims 5 and 6. Claims 5 and 6 do not specifically refer to "purified", however no objection to these claims was provided on that basis. Accordingly, the objection to claims 5 and 6 should be removed.

VI. Claim 36 Stands Objected for Depending Upon Claim 6

Claim 36 was indicated to be allowable if rewritten in dependent form including all the limitations of the base claim and any intervening claim. (Advisory Action dated 3/25/2010, at page 17, under Remarks.) Claim 36 depends from claim 6. As discussed in Argument V. *supra*., the objection to claim 6 showed be removed.

CONCLUSION

Appellants request that the Board of Patent Appeals and Interferences reverse the outstanding rejections of claims 1, 4, 7-9, 33-35, and 38-54.

Please charge deposit account 13-2755 for fees due in connection with Appellants Reply Brief. If any time extensions are needed for the timely filing of the present Appellants Reply Brief, Appellants petition for such extensions and authorize the charging of deposit account 13-2755 for the appropriate fees.

Respectfully submitted,

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